UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,246	04/02/2001	Sharat Singh	0225-0033.20	4459

33603 7590 09/21/2004

ACLARA BIOSCIENCES, INC.
1288 PEAR AVENUE
MOUNTAIN VIEW, CA 94043

EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,246	SINGH ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17 and 19-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-17 and 19-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 6/10/2004 has been entered. Claims 16-17 and 19-28 are pending.

1. Claims 16-17, 19-21 and 23-28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705) in view of Kline et al. (5,459,078).

Grossman et al. disclose a method of detecting a plurality of different sequences in a target sequence involving a plurality of sequence probes (See column 2, lines 54-56). The probe comprises the features of the e-tag probe as claimed in claims 16-17, 19-21 and 23-28. The probe includes a binding polymer, a polymer chain which imparts to that probe, a distinctive ratio of charge/translational frictional drag and a reporter attached to the binding polymer (See column 20, lines 52-57). The binding polymer is an oligonucleotide including at least 10-20 bases allowing hybridization to the target polynucleotide (See column 6, lines 66-67 and column 7, lines 1-10). Other binding polymers are analogs of polynucleotides, such as deoxynucleotides with thiophosphodiester linkage (See column 7, lines 11-19). The polymer chain has a ratio of charge/translational frictional drag, which is evidenced by a distinctive electrophoretic mobility in a non-sieving matrix (See column 7, lines 50-64). The polymer chain can be polyethylene oxide (PEO) or a polypeptide chain where the chains are attached to different-sequence binding polymers (See column 3, lines 11-18). The teachings suggest that the charge/translational frictional drag is consisted of carbon, hydrogen, oxygen, phosphorus, nitrogen, sulfur and boron as recited in claim 24. The label refers to a fluorophore or chromophore (See column 6, lines 39-44). The features of Grossman et al.'s probe suggest the features of the claimed e-tag probe.

Grossman et al do not disclose the set of electrophoretic probe in which the oligonucleotide portion is attached with a capture ligand.

Kline et al. disclose a competitive digoxin assay method (See the Abstract). A test sample suspected of containing the analyte of interest may be contacted with the capture reagent to form a charged capture reagent/analyte complex. The complex is then contacted to the oppositely charged solid phase to attract, attach and immobilize the capture reagent/analyte complex (See the Abstract). The test sample can be derived from any desired source (See column 8, lines 5-18). The analyte can be any substance for which there exists a naturally occurring specific binding member or for which a specific binding member can be prepared (See column 8, lines 19-32). The specific binding pair can be biotin and avidin, and complementary nucleotide sequences including probe and capture nucleic acid sequence used in DNA hybridization assays to detect a target nucleic acid sequence (See column 7, lines 37-53).

One of ordinary skill in the art would have been motivated to apply the binding pair biotin and avidin to the nucleic acid probe of Grossman to make the electrophoretic probes for detecting the presence of absence of one or more of a plurality nucleic sequence in a sample. Kline et al. disclose that the invention is not limited to immunoreactive assay and any assays using specific binding reactions between the analyte and assay reagents can be performed (See column 7, lines 28-33) and the ion-capture technique increases the potential number of complexes that can be immobilized on a solid support. It would have been prima facie obvious to make the set of electrophoretic probes with a capture ligand for detecting the presence or absence of one or more of a plurality nucleic acid sequence in a sample.

The response argues that Kline et al. disclose an immunoassay employing a soluble capture reagent comprising multiple binding compounds, such as analyte-specific antibodies bound to an anionic polymer, in Kline, a charged capture reagent is combined with an oppositely

charge solid phase to remove binding compound-analyte complexes from a reaction mixture for detection, whereas in Applicant's invention, charged capture agents are combined with unreacted electrophoretic probes and cleavage products thereof to give them a charge opposites of that of released eTag reporters so that they are not electrophoretically separated together. However, although the goals for using the charged opposite to capture a subject is different, but the motivation of using the charged opposite to capture a subject is the same as set forth in the Office action as that discussion of the ion-capture technique increases the potential number of complexes that can be immobilized on a solid support. Thus, it would have been prima facie obvious to make the set of electrophoretic probes with a capture ligand for detecting the presence or absence of one or more of a plurality nucleic acid sequence in a sample. Therefore, the rejection is maintained.

2. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705) in view of Kline et al. (5,459,078), as applied to claims 16-17, 19-21 and 23-28 above, and further in view of Huie et al. (5,470,967).

The teachings of Grossman et al. and Kline et al. are set forth in section 1 above. None of the references discloses that said oligonucleotide has at least on nuclease resistant linkage

Huie et al. disclose phosphodiester linkage in oligonucleotide analogs (See column 3, lines 59-62) and phosphorothioate diester shows increased resistance to nuclease (See column 3, lines 59-67). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to use phosphodiester linkage as indicated by Huie et al. in the oligonucleotide probe of Grossman et al. to resist nuclease activity because the use of modified linkage within the oligonucleotide makes them nuclease resistant (See column 3, lines 63-67).

The response filed February 21, 2003 has been discussed in the Office action mailed May 21, 2004. Based upon the same reasons as discussed in the Office action mailed May 21, 2004, the rejection is maintained.

3. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705 (1995)) in view of Kline et al. (5,459,078) as applied to claims above, and further in view of Ullman et al. (6,251,581B1 (2001))

The teachings of Grossman et al. and Kline et al. are set forth in section 1 above.

Grossman et al. and Kline et al. do not disclose the detectable labels, which are the compounds, listed in claim 29.

Ullman et al. disclose a method for determining an analyte in a medium (See the Abstract). The method applies a chemiluminescent compound associated with a specific binding pair member (See column 4, lines 54-65 and column 5, lines 8-14). The compound has the same structure as the compound listed in claims 29 (See column 42-58).

One of ordinary skill in the art at the time of the invention was made would have been motivated to apply the chemiluminescent compound of Ullman et al. to the probe of Grossman et al. in order to construct the set of electrophoretic tag probe of instant invention. Ullman et al. disclose a chemiluminescent compound to bind to a specific binding pair complex so that the detection may be performed without heating the medium to produce light and conducted at a constant temperature (See column 7, lines 28-31). If the analytes are proteins, by avoiding heating, protein analytes would not be inactivated and thus the sensitivity of the method is increased. It would have been prima facie obvious to apply the fluorescent molecules to the electrophoric release tag to construct the set of electrophoretic tag probe to avoid inactivating

protein analytes. Thus it would have been prima facie obvious to apply the fluorescent molecules to the electrophoric release tag to construct the set of electrophoretic tag probe.

As set forth in section 1 above, the rejection of claims 16-17, 19-21 and 23-28 over Grossman (5,470,705) in view of Kline et al. (5459078) is maintained.

The response argues that the composition of appplicants' invention comprises pluralities of such compound that form distinct pearks in an electropherogram upon electrophoretic separation, while the Ullman et al.'s objective is to provide a homogeneous assay based solely on optical detection. However, all fluorescent compounds are used in detection, Thus, it would have been prima facie obvious to apply the fluorescent molecules to the electrophoric release tag to construct the set of electrophoretic tag probe. Therefore, the rejection is maintained.

Summary

4. No claims are allowable

5. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung
September 13, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
9/16/04